The use of Doppler velocimetry of the umbilical artery before 24 weeks' gestation to screen for high-risk pregnancies

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Abstract ***Objective.*** **To describe the prevalence and natural history of absent end-diastolic velocities (AEDV) in the umbilical artery of the fetus between 16 and 24 weeks' gestation, and to evaluate its role as a screening test.**

Design. **Population-based descriptive study.**

Setting. **Tygerberg Hospital, Tygerberg, South Africa. The hospital serves a population from the lower socio-economic bracket.**

Subjects. **Doppler velocimetry was performed at routine ultrasound examinations for confirmation of gestational age in 496 women.**

Main outcome measures. **The occurrence of perinatal death, small-for-gestational-age (SGA) babies and proteinuric hypertension.**

Results. **Forty-four (8,9%) patients had AEDVs at the first examination, but AEDV persisted in only 1. In this case, severe proteinuric hypertension developed unexpectedly at 29 weeks' gestation and the fetus needed delivery because of persistent late decelerations of the fetal heart rate pattern. There was a significant association between the group with AEDV at first examination and the development of proteinuric hypertension (P <0,05), but no association with SGA babies. The association with proteinuric hypertension was too weak to be of clinical use.**

Conclusion. **Doppler velocimetry of the umbilical artery, performed along with routine ultrasound examination to confirm gestational age, is not of use as a screening test for identifying high-risk pregnancies.**

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Fetuses with persistent absent end-diastolic velocities (AEDVs) of the umbilical artery have been shown to have very high mortality and morbidity rates.[1] In women with recurrent fetal losses, AEDV was present for an average of 5 weeks before fetal complications set in, and mostly from the first examination at around 22 weeks.[1] Therefore, Doppler velocimetry performed in the middle of the second trimester might be of use as a screening test to identify high-risk pregnancies. However, these findings may not be applicable to a lower risk population, and general application of the findings may be harmful.

For this reason, a cohort analytical study of Doppler velocimetry was undertaken in women who were representative of the general population served by Tygerberg Maternity Services (TMS), and who presented for routine ultrasound evaluation. The study aimed to describe the prevalence and natural history of AEDV of the fetus in a general pregnant population and to evaluate its possible role as a screening test.

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Material and methods

The first 10 women who presented daily for routine ultrasound screening between 16 and 24 weeks' gestation, from February to May 1990, were asked to participate in the study. Umbilical artery velocity waveforms were obtained with a 4 MHz continuous-wave Doppler ultrasound instrument and analysed by means of a spectrum analyser (Doptek 9000; Doptek, Chichester, England). All Doppler examinations were performed by a single observer. A 200-Hz thump filter was used to eliminate the low frequencies obtained from movements of the arterial wall. The umbilical artery waveform was obtained transabdominally with the patient in the left lateral position and the hand-held continuous-wave transducer adjusted to obtain the best umbilical signal identified by its characteristic appearance. Recordings of the waveforms were taken only when the pattern was stable, indicative of fetal apnoea and the absence of fetal activity. Once a steady signal had been obtained, the Doppler signal was frozen and the resistance index (RI) measured in five consecutive waveforms; the mean result was then calculated. The RI was regarded as abnormal if it was greater than the 95th centile of the Tygerberg Hospital standard curve.[2]

The Doppler velocimetric findings were withheld from the clinicians and the women were followed up in the routine manner. If AEDV was detected, the Doppler velocimetry examination was repeated at the routine visits until it returned to normal or the woman delivered.

Antenatal and neonatal complications were recorded from the hospital records. Each patient was managed according to standard protocols relating to their specific problem. The clinical signs which determined fetal jeopardy were a decrease in the symphysis-fundal measurement of the uterus, decreased perception of fetal movements and a deterioration in the mother's clinical situation, e.g. raised blood pressure or the onset of proteinuria.

Hypertensive conditions were defined according to the specifications of Davey and MacGillivray.[3] Severe proteinuric hypertension was defined as a blood pressure greater than 160/110 mmHg and 3+ or more proteinuria on dipsticks. Small-for-gestational-age (SGA) babies were defined as weighing less than the 10th centile for gestational age according to the growth curves for international reference.[4]

The data were analysed by means of the χ^2-test (with Yates correction), or Fisher's exact test where the numbers were small, to compare proportions; Student's t-test was used to assess normally distributed continuous variables. A value of $P < 0,05$ was regarded as significant. To estimate the value of Doppler velocimetry of the umbilical artery and uterine vessels as screening tests, the sensitivity, specificity and positive predictive value were calculated with an overall assessment of the test expressed by means of the kappa index.[5] A kappa

index combines the predictive power of the test with the prevalence of the disease in the study population. A kappa index below 0,4 indicates results that are no better than chance alone, a value of 0,4 - 0,75 a test moderately better than chance, and values of more than 0,75 an excellent screening test.

The study was approved by the Tygerberg Hospital Ethics Committee and before entry into the study all patients gave informed consent.

Results

Five hundred and twenty-nine women initially entered the study. However, 23 were transferred to other hospitals during their pregnancy and 9 were lost to follow-up. These women were excluded from further analysis.

A total of 496 women completed the study and form the study group. The population was representative of the population directly served by TMS (Table I).

TABLE I.
Comparison between the study group and the general population served by TMS

	Study group (496)	TMS population (6 851)
Primigravidas	184 (37%)	2 638 (39%)
Mean birth weight (g)	2 980 ± 605	2 913 ± 663
Mean gestational age (wks)	38,0 ± 2,7	38,2 ± 2,9*
SGA	39 (8%)	258 (8%)*
Proteinuric hypertension	50 (10%)	534 (8%)
Perinatal deaths	14 (2,8%)	227 (3,3%)†

* 3 786 patients had accurate gestational assessment by early ultrasound and only this group were used for these calculations.
† Deaths from 500 g to 28 days postpartum.

In the population studied, 44 (8,9%) fetuses had AEDV at screening and 14 (2,8%) abnormal Doppler velocimetry values. The distribution of AEDV and abnormal Doppler values with regard to gestational age is shown in Figs 1 and 2.

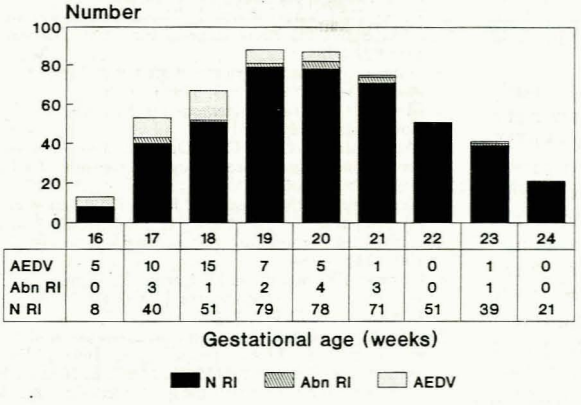

FIG. 1.
Distribution of gestational age in women presenting for routine ultrasound and having Doppler velocimetry (N RI = normal resistance index, Abn RI = abnormal resistance index).

In only 1 woman was the AEDV persistent (prevalence 0,2%). In all the remaining women end-diastolic velocities were present at 24 weeks' gestation. The woman in whom AEDV was persistent in the fetus, was a 21-year-old primigravida who had booked at 18 weeks' gestation and in whom no risk factors had been

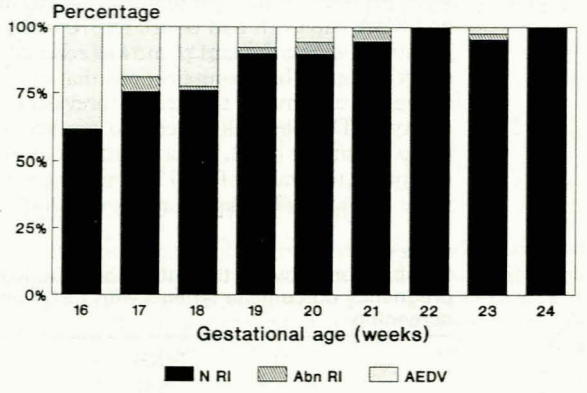

FIG. 2.
Percentage of normal RIs, abnormal RIs and AEDVs per gestational age in women screened between 16 and 24 weeks' gestation (N RI = normal resistance index, Abn RI = abnormal resistance index).

detected. Her antenatal care was uneventful until 29 weeks when she presented with headache, visual flashes and abdominal pain; she felt faint and had had a fit-like episode in which she did not lose consciousness. Her blood pressure was 170/120 mmHg on admission and she had 2+ proteinuria. The special investigations (haematocrit, platelet count, serum creatinine, liver function tests and mid-stream urine culture) were all within normal limits. She received a loading dose of magnesium sulphate (4 g intravenously slowly and 10 g intramuscularly) shortly thereafter. Her blood pressure stabilised quickly and the proteinuria disappeared. However, 12 hours later, repeated late decelerations were detected on monitoring of the fetal heart rate. Her blood pressure at this time was 130/100 mmHg. An emergency caesarean section was performed for fetal reasons. The baby weighed 1 100 g with a 5-minute Apgar score of 6 and spent 135 days in neonatal intensive care with multiple problems. The major complications were intracranial bleeding and bronchopulmonary dysplasia. The postpartum course of the mother was uneventful.

The outcome of the pregnancies is shown in Table II. There was a significant association between AEDV and the development of proteinuric hypertension ($P = 0,033$, odds ratio (OR) 2,6, 95% confidence interval (CI) 1,06 - 6,07). If those patients who developed severe proteinuric hypertension are analysed separately, the association becomes stronger — 7 (15,9%) in the AEDV group compared with 20 (4,4%) in the EDV group ($P = 0,006$, OR 4,0, 95% CI 1,4 - 11,0).

The ability of Doppler velocimetry to predict proteinuric hypertension had a sensitivity of 18%, a specificity of 92%, a positive predictive value of 20,5%, and a negative predictive value of 90,9%. The prevalence of proteinuric hypertension was 10%; the kappa index was therefore a low 0,107.

Doppler velocimetry of the umbilical artery detects problems related to placental vascular insufficiency, namely intra-uterine growth retardation and proteinuric hypertension,[6] and detects these problems earlier than other methods.[1] Therefore, abnormal Doppler velocimetry results should predict intra-uterine growth retardation and proteinuric hypertension. Consequently, SGA babies and proteinuric hypertension can be used as end points for screening. In the AEDV population studied, 9 women had proteinuric hypertension and 3 SGA babies (2 were coincident), i.e. there were 10 women with complications in whom end points were reached. In the population where end-diastolic velocities

were present 41 had proteinuric hypertension and 37 had SGA babies (8 had both), i.e. 70 women had complications where the end point was reached. In the total study group 80 had complications that one might expect Doppler velocimetry to predict (prevalence 16%). The ability of Doppler velocimetry to predict complications had a sensitivity of 12,5%, a specificity of 91,8%, a positive predictive value of 22,7%, and a negative predictive value of 84,5%. The kappa index was 0,053.

TABLE II.
Comparison between the antenatal complications and pregnancy outcome in fetuses with AEDV and EDV at screening

	AEDV (44)	EDV (437)	*P*
Antenatal complications			
Hypertension only	1 (2%)	10 (2%)	
Proteinuric hypertension	9 (20%)	41 (9%)	< 0,05
Abruptio placentae	1 (2%)	1 (0,2%)	
Spontaneous preterm labour	4 (9%)	31 (7%)	
Premature rupture of membranes	2 (5%)	18 (4%)	
Caesarean section	8 (18%)	51 (12%)	
Birth weight (g)	2 875 ± 625	2 989 ± 607	
Gestational age (wks)	37,9 ± 2,6	38,0 ± 2,7	
SGA babies	3 (7%)	36 (8%)	
Gestational age			
< 34 weeks	4 (9%)	13 (3%)	
34 - 37 weeks	6 (14%)	53 (12%)	
Abortions	0	5 (1%)*	
Perinatal deaths	0	9 (2%)†	

* Abortion = gestational age less than 24 weeks, all weighed 500 g or more.
† Perinatal death = gestational age 24 weeks or more until 28 days postpartum.

Discussion

In this study 496 women were followed prospectively after Doppler velocimetry was carried out at routine ultrasound examination to confirm gestational age. The population studied was representative of the general population served by TMS, although it might have been at a slightly lower risk because all the women booked early.

It was found that AEDV before 24 weeks is fairly common (8,9%). This finding had previously been reported.[7-9] There was an association between AEDV of the umbilical artery early in pregnancy and severe proteinuric hypertension, although this was not clinically useful. The finding of this association supports the hypothesis that the development of the placental vascular lesion, which deprives the fetus, is the primary vascular disease and the manifestation of hypertension in the mother is secondary to this.[6] However, Newnham *et al.*,[7] in the only other study reported where Doppler velocimetry was performed in the middle of the second trimester as a screening test, did not find an association; these results will therefore need to be confirmed by other workers. There was no association with SGA babies in this study but an association was found by Newnham *et al.*[7] However, despite the proven association of abnormal Doppler velocity waveforms and SGA babies, screening of the general population in the third trimester for SGA babies has not been found to be of value.[7,10-13]

It is possible that AEDV in early pregnancy is something which comes and goes and may not have any specific significance. This however, does not appear to be the case because in studies where normal pregnant women were followed serially to determine reference values, this was not observed.[2,14]

Persistent AEDV after 24 weeks was rare in this study and the only patient in whom AEDV persisted had a poor outcome. The prevalence of AEDV in the general population in the third trimester has been reported to be 0,28%,[11] 0,39%[12] and 0,37%,[13] which is very similar to the prevalence of persistent AEDV of 0,20% found in this study. AEDV was associated with a poor prognosis in two of the three studies. Beattie and Dornan[11] found that 2 of the 3 fetuses where AEDV persisted died. Of the 3 unexplained stillbirths in their study all had abnormal Doppler indices. Schulman *et al.*[12] found 1 patient who, although originally clinically normal, needed delivery at 29 weeks' gestation for recurrent late decelerations. However, Hanretty *et al.*[13] reported 10 cases of AEDV in the third trimester when screening a general population at 26-30 weeks and 34-36 weeks, but only 2 were persistent. These 2 mothers and babies had no problems. Despite the last study's findings, AEDV after 24 weeks should probably be considered clinically important.

In this study, where the population was representative of the general population served by TMS, Doppler velocimetry was not found to be of use in screening for the complications of pregnancy that it might be expected to predict, namely intra-uterine growth retardation and proteinuric hypertension.

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